REMARKS

This is in response to the office action mailed February 12, 2007 in the above identified application. Applicants request a two month extension of time for response and enclose the required fee. Applicants are concurrently filing an RCE and the requisite RCE fee herewith to ensure consideration of the present amendment.

Claims 1-4 are currently pending. By this amendment, Claim 3 has been canceled without prejudice to presenting the subject matter thereof in a further application.

Claim 1 has been amended to more clearly and precisely define the subject matter of the claimed invention.

The specification has been objected to as containing new matter. An appropriate amendment to the specification has been made in accordance with the Examiner's requirement.

Claims 1-4 remain rejected under 35USC §103(a) as obvious over the combination of Hirsch et al and Krska et al.

Applicants respectfully submit that the examiner's maintained rejection is in error. Hirsch et al. clearly discounts the value of a 2D-gel separation for identifying proteins to which a patient with cancer raises autoantibodies, as compared to an individual without cancer. Careful examination of Hirsch et al. clearly shows that Hirsch et al. actually teaches away from the current invention. In reviewing the 2D Western blots of figures 1 and 3, Hirsch et al. conclude that other than the spots at 65kDa, all other staining was 'the usual background' i.e. of no value as information concerning the discovery and identification of proteins to which patients with cancer raise

autoantibodies. In so doing it is clear that Hirsch et al. do not disclose the currently claimed invention and provide no guidance to one of skill in the art as to how to arrive at it. Indeed Hirsch et al. positively discourage such a skilled person to even try by teaching that any spots unrelated to proteins previously discovered by 1D Western blot are merely "the usual background".

The examiner asserts that the teaching of Hirsch et al. must be combined with that of Krska et al. and the two publications taken as a whole. In the first case the applicants respectfully suggest that there is no such guidance in Hirsch et al. or Krska et al. to consult the other, and that, since these two studies are in completely unrelated fields, they do not represent the same art. Moreover, even taken together they fail to teach or suggest the presently claimed invention.

Even assuming arguendo that the skilled person looking to find better ways of identifying proteins to which a patient with cancer would raise antibodies would consider the field of bacterial evolution of the Dnak protein and characterization of a monoclonal antibody thereto, she would still not have arrived at the present invention.

Krska et al. is concerned with characterizing a monoclonal antibody raised against an exogenous antigen. This is completely unrelated to the production of antibodies against an autologous protein, as is the case in Hirsch et al. and which only looks at 1D separation as in the current invention in which 2D separation is used to identify cellular antigens to which a cancer patient raises autoantibodies. It is well understood in the field of immunology that the mammalian immune system is designed to act against exogenous

(non-self) antigens. Conversely, there should be no response to autologous (self) antigens which are generally ignored by the immune system. Where antibodies are raised to autoantigens, the individual normally suffers from an autoimmune disease, such as rheumatoid arthritis, scarlet fever or lupus.

In oncology, it is believed that an autoimmune response is triggered by abnormal expression and/or excretion and proteolysis of self-proteins which are then rendered antigenic. The problem to be solved was how to identify these newly created self-antigens and provide them as ready means for diagnosing cancer based on detection of autoantibodies to them in individuals as provided in the present invention.

Thus, a combination of Krska et al. and Hirsch et al. fails to provide such a method or suggest such a method based on the 2D Western blotting of unknown proteins screened with sera containing unknown antibodies. In Hirsch et al. *a priori* knowledge of the target protein is required from a 1D Western blot before performing 2D Western blot, and any staining of spots inconsistent with the prior identified antigen are specifically discounted as background. Krska et al. is silent on the level of background staining and so provides no further guidance that *a priori* knowledge of the antigen is required. To the contrary, Krska et al. requires absolute knowledge of the target antigen, since it must first be used to immunize BALB/c mice or New Zealand white rabbits to provide the sera for use in Western blotting.

In view of the amendments to the claims and the remarks above, it is believed that the rejections have been overcome. Applicants respectfully solicit a Notice of Allowance.

Applicants have requested a two month extension of time. The Commissioner is hereby authorized to charge the extension fee and any additional payment, or credit any overpayment, to Deposit Account No. 01-2300, **referencing Docket Number 108140.00015.**

Respectfully submitted,

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FEE CALCULATION

Any additional fee required has been calculated as follows:

X If checked, "Small Entity" status is claimed.

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT	(Column 2) HIGHEST NO. PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA
TOTAL CLAIMS	3 MINUS	21	= 0
INDEP CLAIMS	1 MINUS	3	= 0
☐ FIRST PRESENTATION OF MULTIPLE DEP. CLAIM			

SMALL ENTITY RATE	SMALL ENTITY ADD'L FEE	OR	LARGE ENTITY RATE	LARGE ENTITY ADD'L FEE
x $25	$0.00		x $50	$
x $100	$0.00		x $200	$
+ $180	$0.00	OR	+ $360	$
	$0.00			$

The U.S. Patent and Trademark Office is hereby authorized to charge the current fees and any deficiency or credit any overpayment of fees associated with this communication to Deposit Account No. **01-2300** referencing docket number **108140.00015**.